

Figure 1

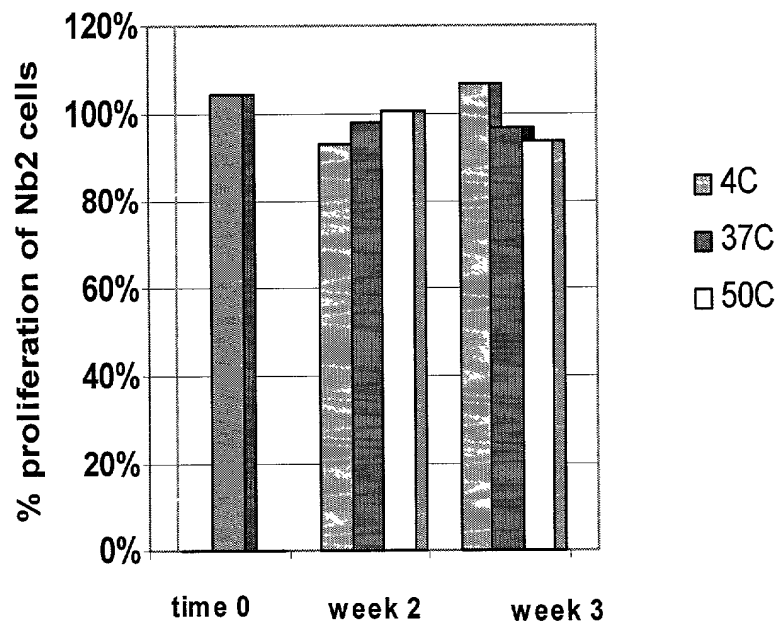


Figure 2

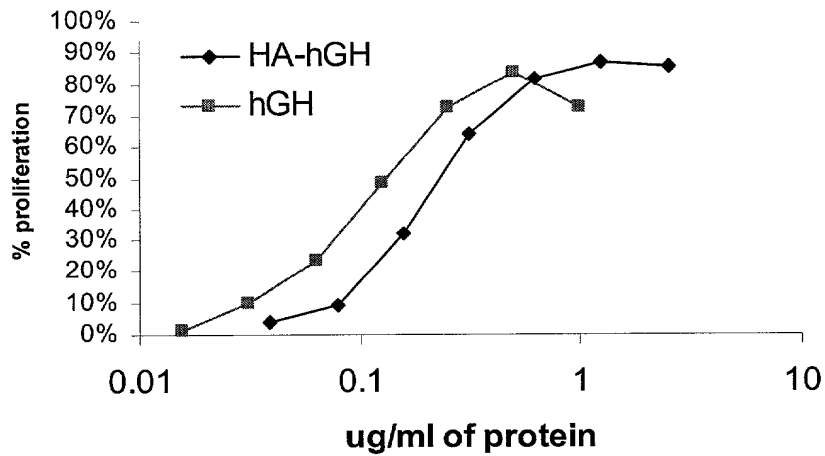


Figure 3A

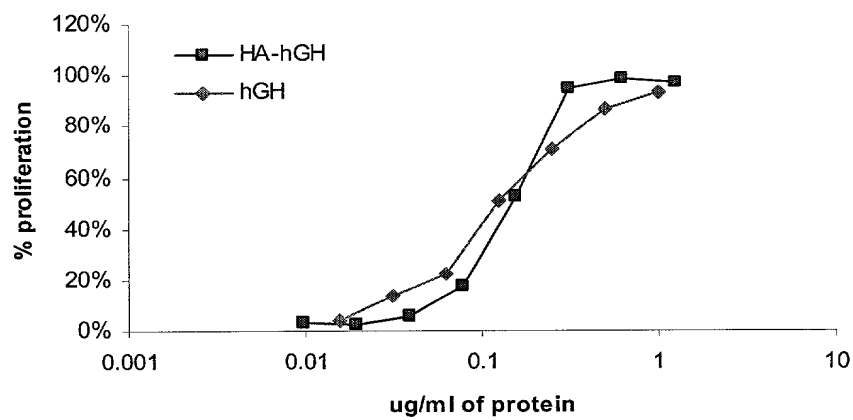


Figure 3B

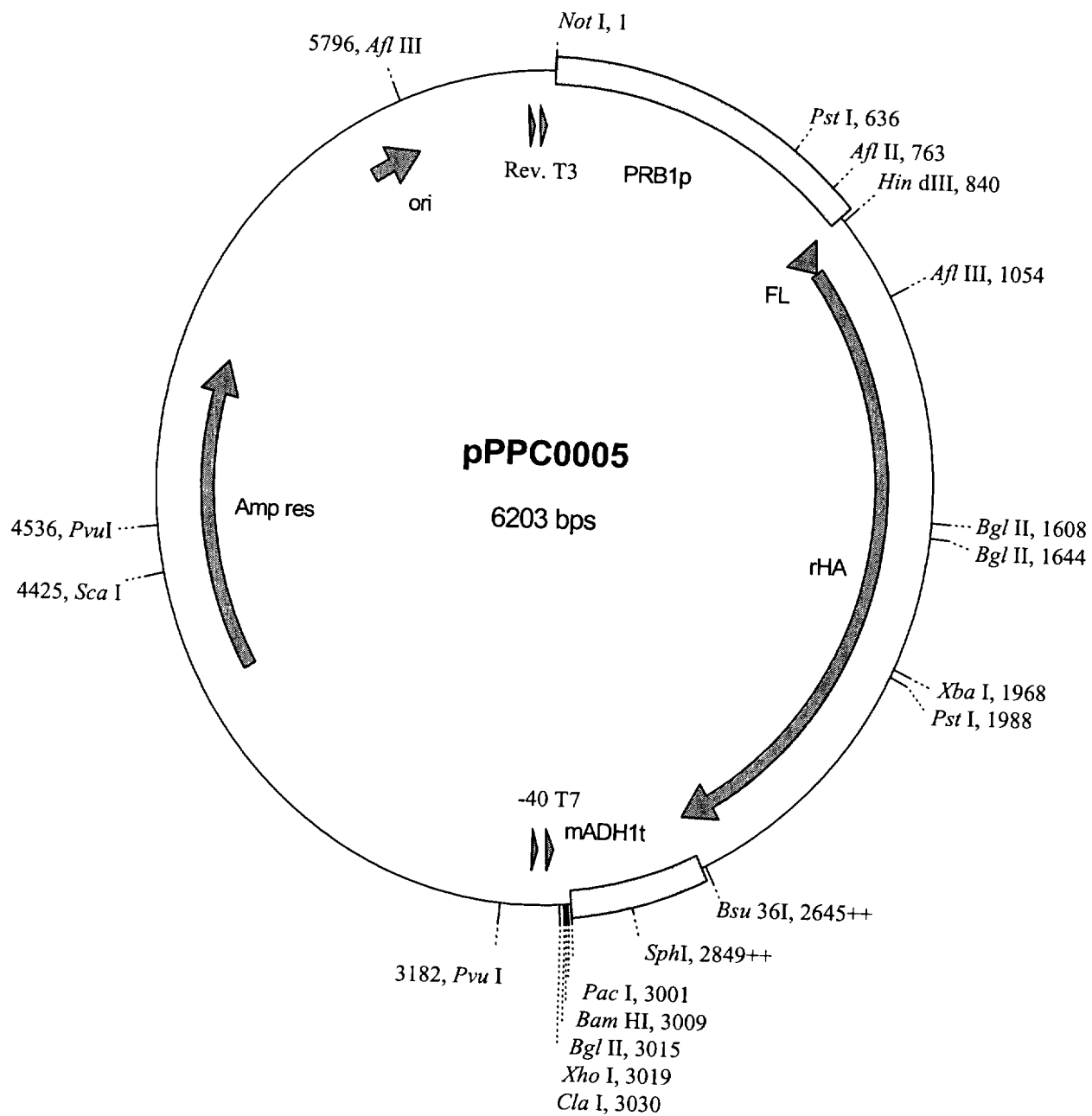


Figure 4

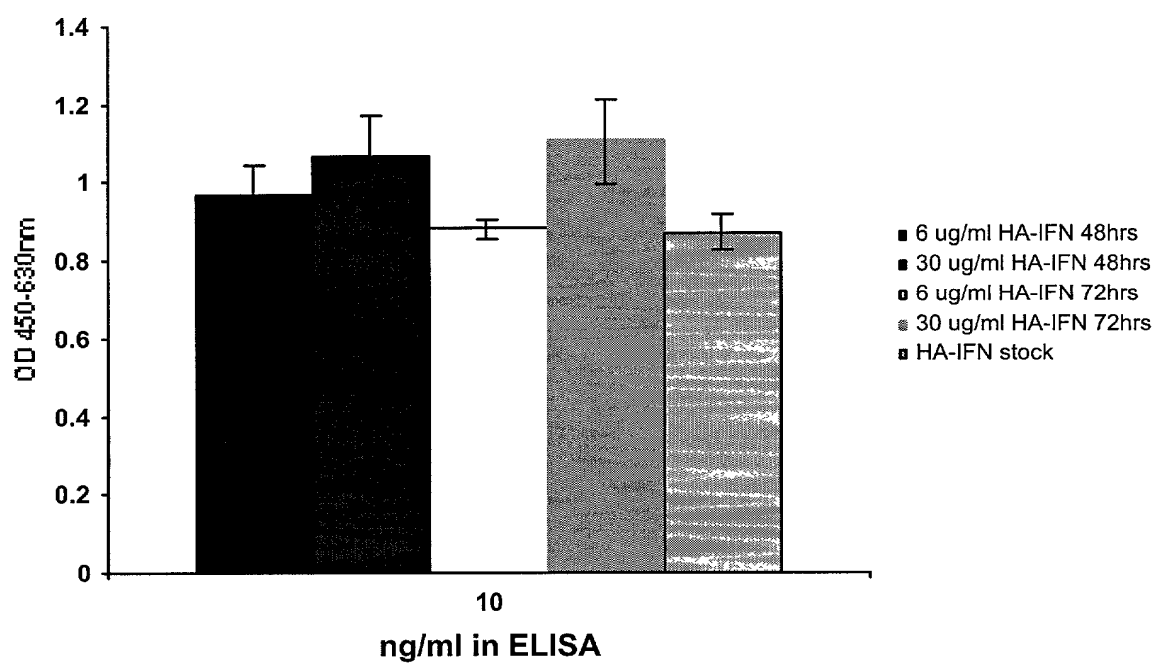


Figure 5

Figure 6

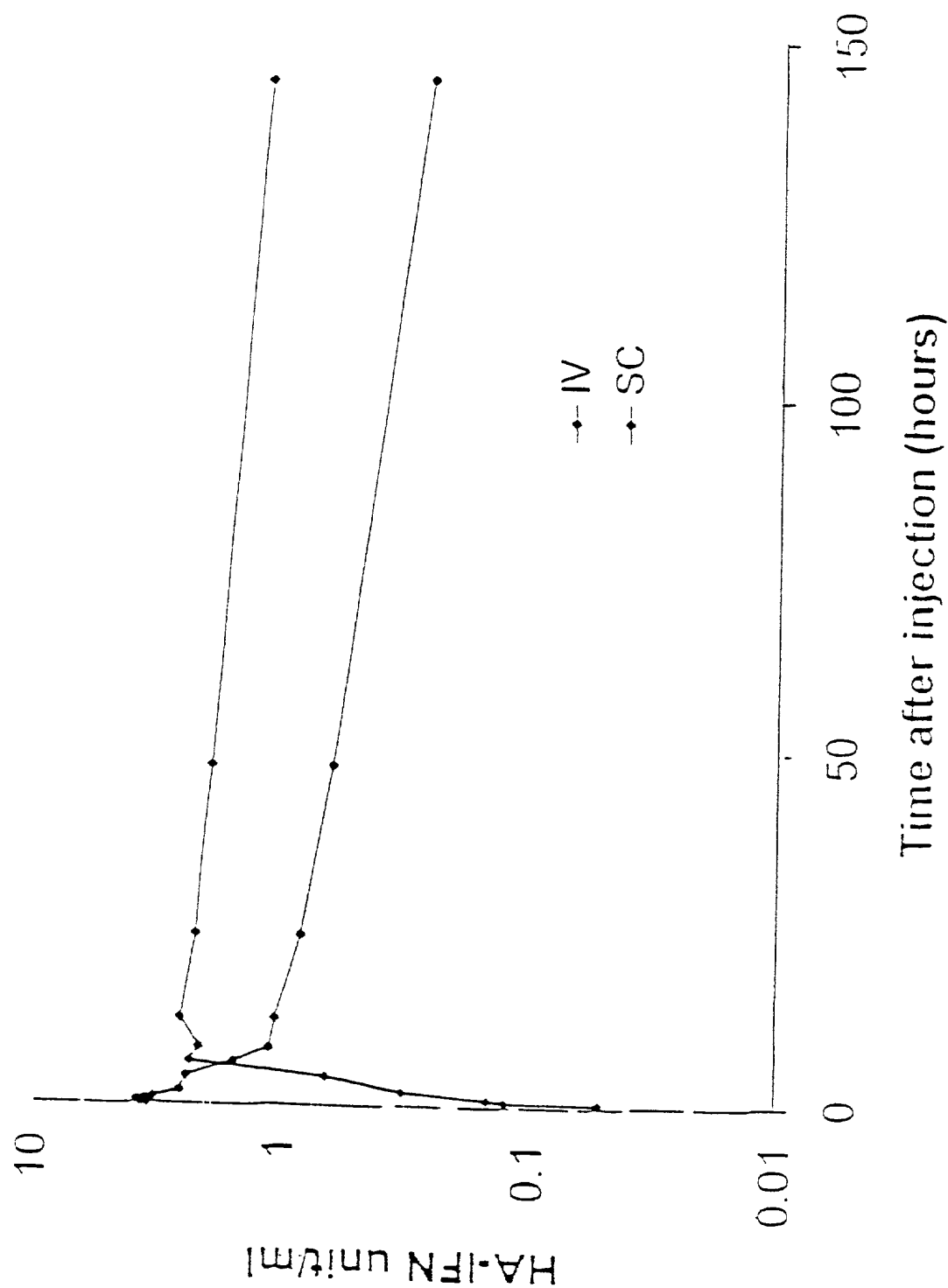
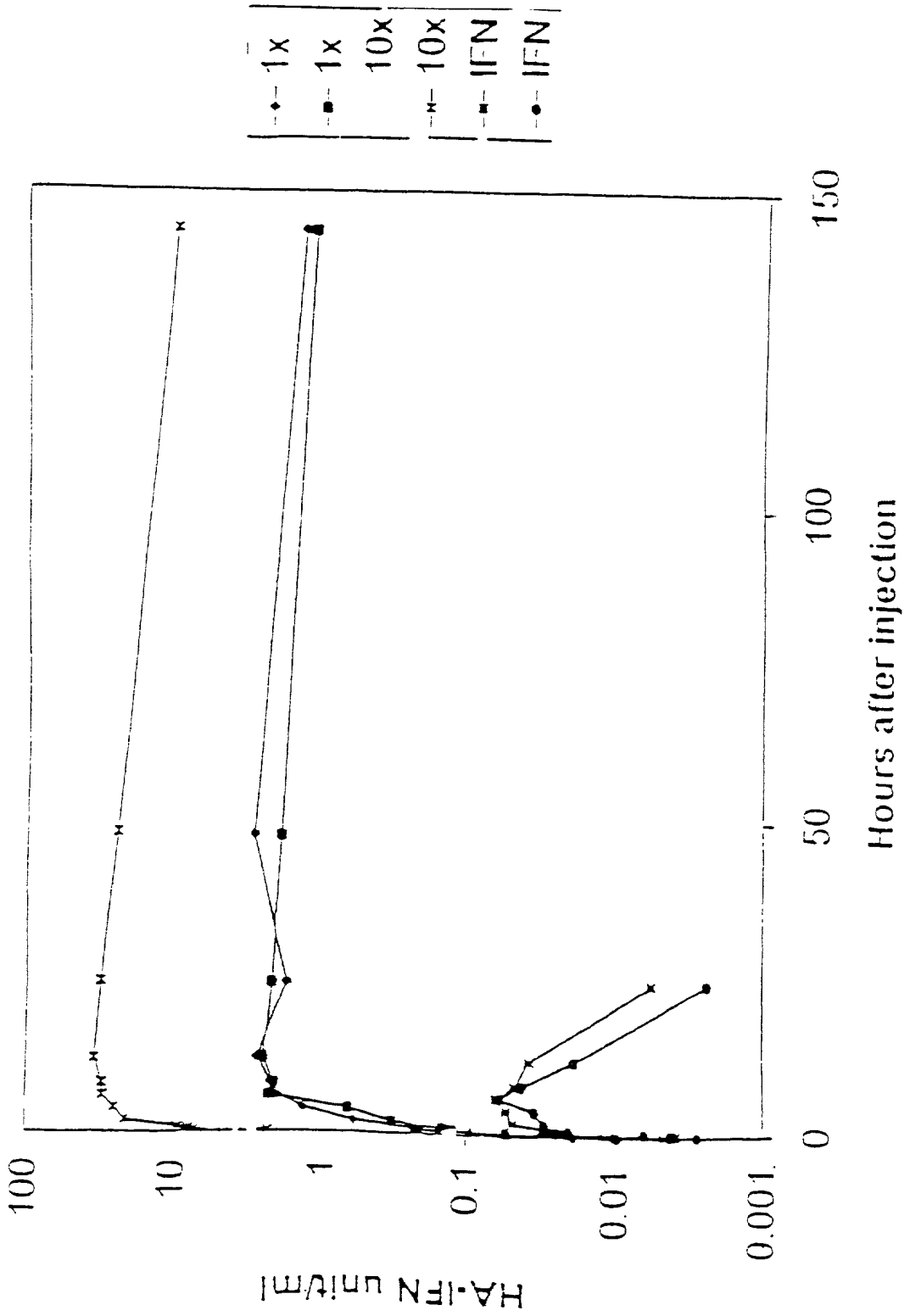


Figure 7



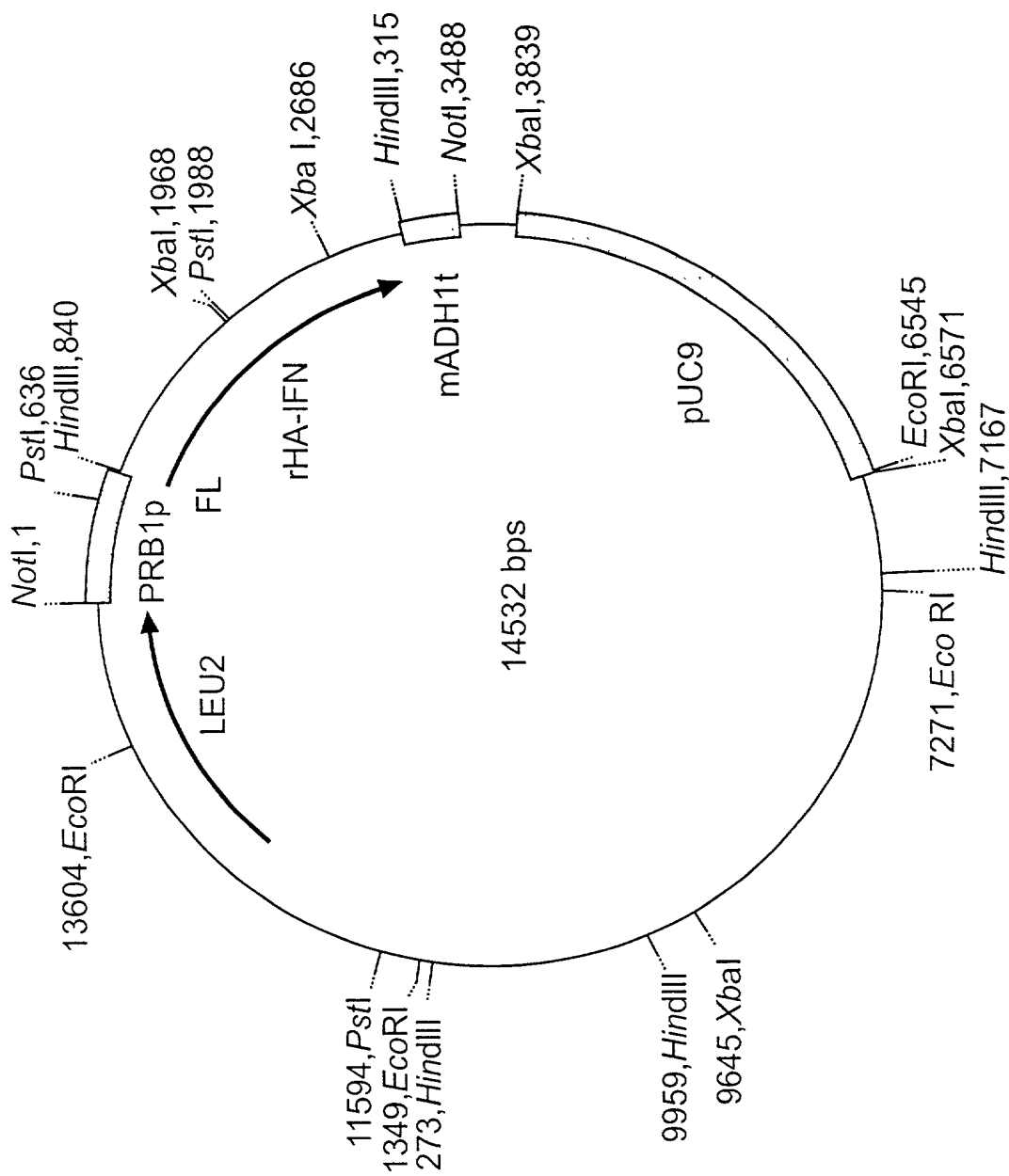


FIG. 8

Figure 9

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1    DAHKSEVAHR FKDLGEENFK ALVLIAFAQY LQQCPFEDHV KLVNEVTEFA
      HHHHH HHH      HHH HHHHHHHHHHH      HHHHH HHHHHHHHHHH

      I                      II                      III
51   KTCVADESAE NCDKSLHTLF GDKLCTVATL RETYGEMADC CAKOEPERNE
      HHHHH      HHHHH HHHHH      HHHH H      HHHH

101  CFLQHKDDNP NLPRLVRPEV DVMCTAFHDN EETFLKKYLY EIARRHPYFY
      HHHH      H      HHHHHHHHH      HHHHHHHHH HHHHH

      IV
151  APELLFFAKR YKAAFTECCO AADKAACLLP KLDELRLDEGK ASSAKQRLKC
      HHHHHHHHHHH HHHHHHHHH      HHHHH HHHHHHHHHHH HHHHHHHHHHH

      V
201  ASLQKFGERA FKAWAVARLS QRFPKAEFAE VSKLVTDLTK VHTECCHGDL
      HHHHH      HH HHHHHHHHHHH HH      HHH HHHHHHHHHHH HHHHHH HH

      VI                      VII
251  LECADDRADL AKYICENODS ISSKLKECCE KPLLEKSHCI AEVENDEMPA
      HHHHHHHHHHH HHHHH      HHHHH      HHHHHHH H

301  DLPSLAADFV ESKDVCKNYA EAKDVFLGMF LYEYARRHPD YSVVLLLRLLA
      HHHH      HHHHHH      HHHHHHH HHHHHH      HHHHHHHHH

      VIII
351  KTYETTLKLC CAAADPHECY AKVFDEFKPL VEEPQNLIKQ NCELFEQLGE
      HHHHHHHHHHH      HH      H      HHHHH HHHHHHHHHHH HHHHHHH

      IX
401  YKFQNALLVR YTKKVPQVST PTLVEVSRNL GKVGSKCCKKH PEAKRMPCAE
      HHHHHHHHHHH HHHH      H HHHHHHHHHHH      HHH      HHHHHHHHH

      X                      XI
451  DYLSVVLNQL CVLHEKTPVS DRVTKCCTES LVNRRPPCFSA LEVDETYVPK
      HHHHHHHHHHH HHHHH      HHHHHHHHH      HHHHHHHHH

501  EFNAETFTFH ADICTLSEKE RQIKKQTALV ELVKHKPKAT KEQLKAVMDD
      HHH      HHH HHHHHHMEHHH HHH      HHHHHHHHH

      XII
551  FAAFVEKCCK ADDKETCFAE EGKKLVAASQ AALGL
      HHHHHHHHH      HHHH HHHHHHHHHHH HH

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Loop

I Val54-Asn61
 II Thr76-Asp89
 III Ala92-Glu100
 IV Gln170-Ala176
 V His247-Glu252
 VI Glu266-Glu277

Loop

VII Glu280-His288
 VIII Ala362-Glu368
 IX Lys439-Pro447
 X Val462-Lys475
 XI Thr478-Pro486
 XII Lys560-Thr566

Figure 10

a. Randomisation of Loop IV.

151 APELLFFAKR YKAAFTECCQ AADKAACLLP KLDEL RDEGK ASSAKQRLKC
 HHHHHHHHHH HHHHHHHHHH HHHHH HHHHHHHHHHH HHHHHHHHHHH

151 APELLFFAKR YKAAFTECCX XXXXXXCLLP KLDEL RDEGK ASSAKQRLKC
 HHHHHHHHHH HHHHHHHHHH HHHHH HHHHHHHHHHH HHHHHHHHHHH

X represents the mutation of the natural amino acid to any other amino acid. One, more or all of the amino acids can be changed in this manner. This figure indicates all the residues have been changed.

b. Insertion (or replacement) of Randomised sequence into Loop IV.

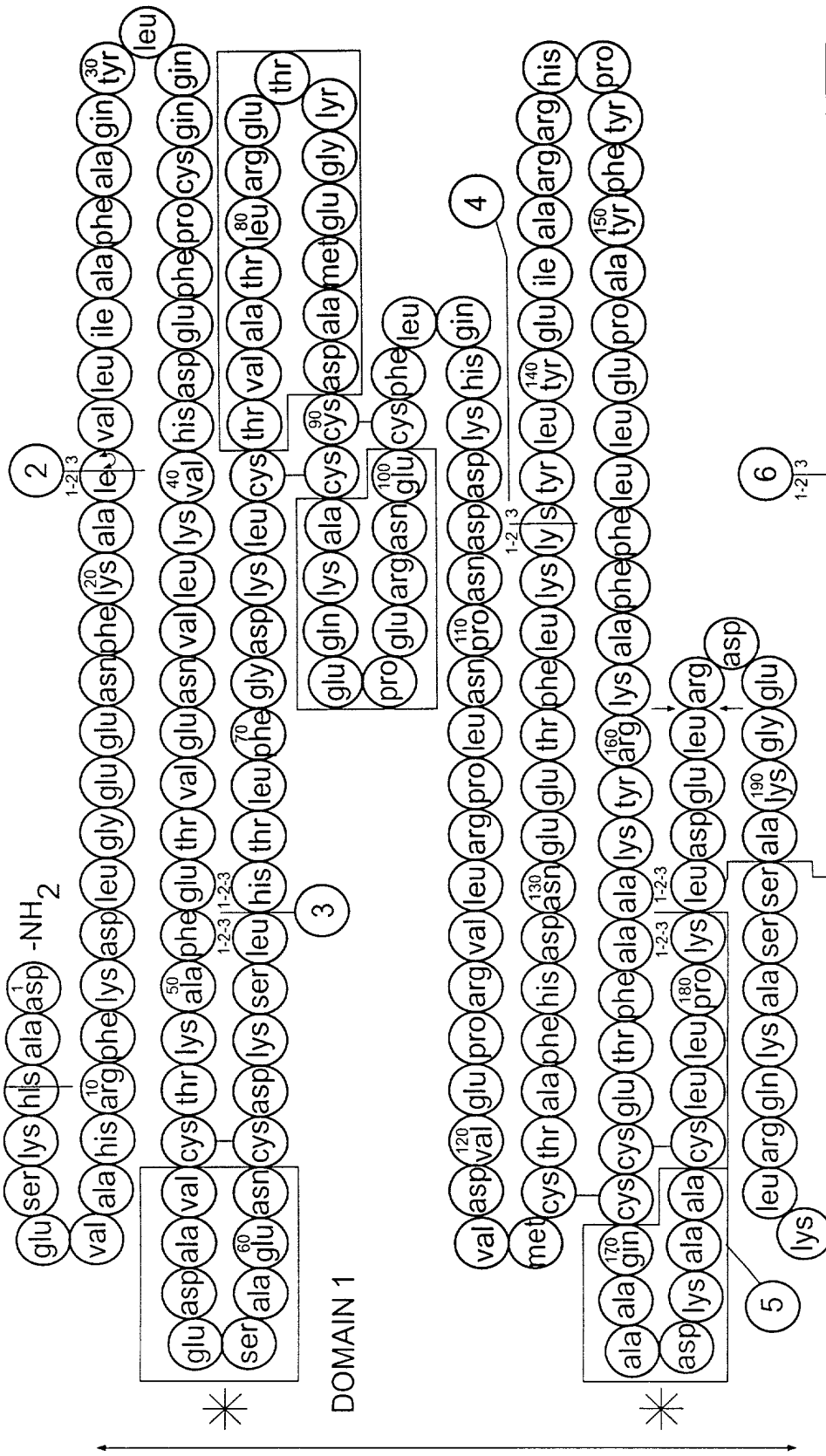
(X)_n



151 APELLFFAKR YKAAFTECCQ AADKAACLLP KLDEL RDEGK ASSAKQRLKC
 HHHHHHHHHH HHHHHHHHHH HHHHH HHHHHHHHHHH HHHHHHHHHHH

The insertion can be at any point on the loop and a length where n would typically be 6, 8, 12, 20 or 25.

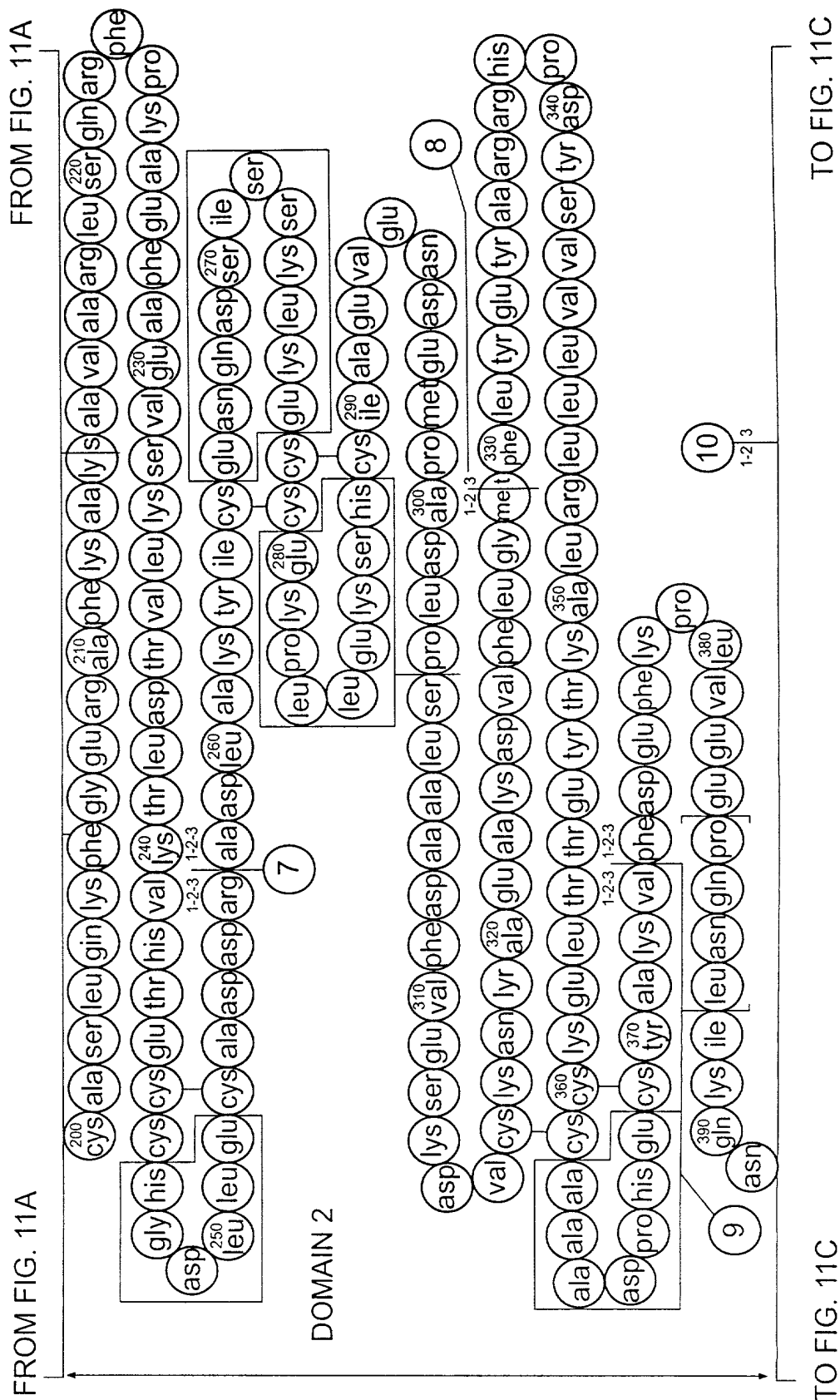
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 101 102 103 104 105 106 107 108 109 110 111 112 113 114 115 116 117 118 119 120 121 122 123 124 125 126 127 128 129 130 131 132 133 134 135 136 137 138 139 140 141 142 143 144 145 146 147 148 149 150 151 152 153 154 155 156 157 158 159 160 161 162 163 164 165 166 167 168 169 170 171 172 173 174 175 176 177 178 179 180 181 182 183 184 185 186 187 188 189 190 191 192 193 194 195 196 197 198 199 200 201 202 203 204 205 206 207 208 209 210 211 212 213 214 215 216 217 218 219 220 221 222 223 224 225 226 227 228 229 230 231 232 233 234 235 236 237 238 239 240 241 242 243 244 245 246 247 248 249 250 251 252 253 254 255 256 257 258 259 260 261 262 263 264 265 266 267 268 269 270 271 272 273 274 275 276 277 278 279 280 281 282 283 284 285 286 287 288 289 290 291 292 293 294 295 296 297 298 299 300 301 302 303 304 305 306 307 308 309 310 311 312 313 314 315 316 317 318 319 320 321 322 323 324 325 326 327 328 329 330 331 332 333 334 335 336 337 338 339 340 341 342 343 344 345 346 347 348 349 350 351 352 353 354 355 356 357 358 359 360 361 362 363 364 365 366 367 368 369 370 371 372 373 374 375 376 377 378 379 380 381 382 383 384 385 386 387 388 389 390 391 392 393 394 395 396 397 398 399 400 401 402 403 404 405 406 407 408 409 410 411 412 413 414 415 416 417 418 419 420 421 422 423 424 425 426 427 428 429 430 431 432 433 434 435 436 437 438 439 440 441 442 443 444 445 446 447 448 449 450 451 452 453 454 455 456 457 458 459 460 461 462 463 464 465 466 467 468 469 470 471 472 473 474 475 476 477 478 479 480 481 482 483 484 485 486 487 488 489 490 491 492 493 494 495 496 497 498 499 500 501 502 503 504 505 506 507 508 509 510 511 512 513 514 515 516 517 518 519 520 521 522 523 524 525 526 527 528 529 530 531 532 533 534 535 536 537 538 539 540 541 542 543 544 545 546 547 548 549 550 551 552 553 554 555 556 557 558 559 560 561 562 563 564 565 566 567 568 569 570 571 572 573 574 575 576 577 578 579 580 581 582 583 584 585 586 587 588 589 590 591 592 593 594 595 596 597 598 599 600 601 602 603 604 605 606 607 608 609 610 611 612 613 614 615 616 617 618 619 620 621 622 623 624 625 626 627 628 629 630 631 632 633 634 635 636 637 638 639 640 641 642 643 644 645 646 647 648 649 650 651 652 653 654 655 656 657 658 659 660 661 662 663 664 665 666 667 668 669 670 671 672 673 674 675 676 677 678 679 680 681 682 683 684 685 686 687 688 689 690 691 692 693 694 695 696 697 698 699 700 701 702 703 704 705 706 707 708 709 710 711 712 713 714 715 716 717 718 719 720 721 722 723 724 725 726 727 728 729 730 731 732 733 734 735 736 737 738 739 740 741 742 743 744 745 746 747 748 749 750 751 752 753 754 755 756 757 758 759 760 761 762 763 764 765 766 767 768 769 770 771 772 773 774 775 776 777 778 779 780 781 782 783 784 785 786 787 788 789 790 791 792 793 794 795 796 797 798 799 800 801 802 803 804 805 806 807 808 809 810 811 812 813 814 815 816 817 818 819 820 821 822 823 824 825 826 827 828 829 830 831 832 833 834 835 836 837 838 839 840 841 842 843 844 845 846 847 848 849 850 851 852 853 854 855 856 857 858 859 860 861 862 863 864 865 866 867 868 869 870 871 872 873 874 875 876 877 878 879 880 881 882 883 884 885 886 887 888 889 890 891 892 893 894 895 896 897 898 899 900 901 902 903 904 905 906 907 908 909 910 911 912 913 914 915 916 917 918 919 920 921 922 923 924 925 926 927 928 929 930 931 932 933 934 935 936 937 938 939 940 941 942 943 944 945 946 947 948 949 950 951 952 953 954 955 956 957 958 959 960 961 962 963 964 965 966 967 968 969 970 971 972 973 974 975 976 977 978 979 980 981 982 983 984 985 986 987 988 989 990 991 992 993 994 995 996 997 998 999 1000



TO FIG. 11B

TO FIG. 11B

FIG. 11A



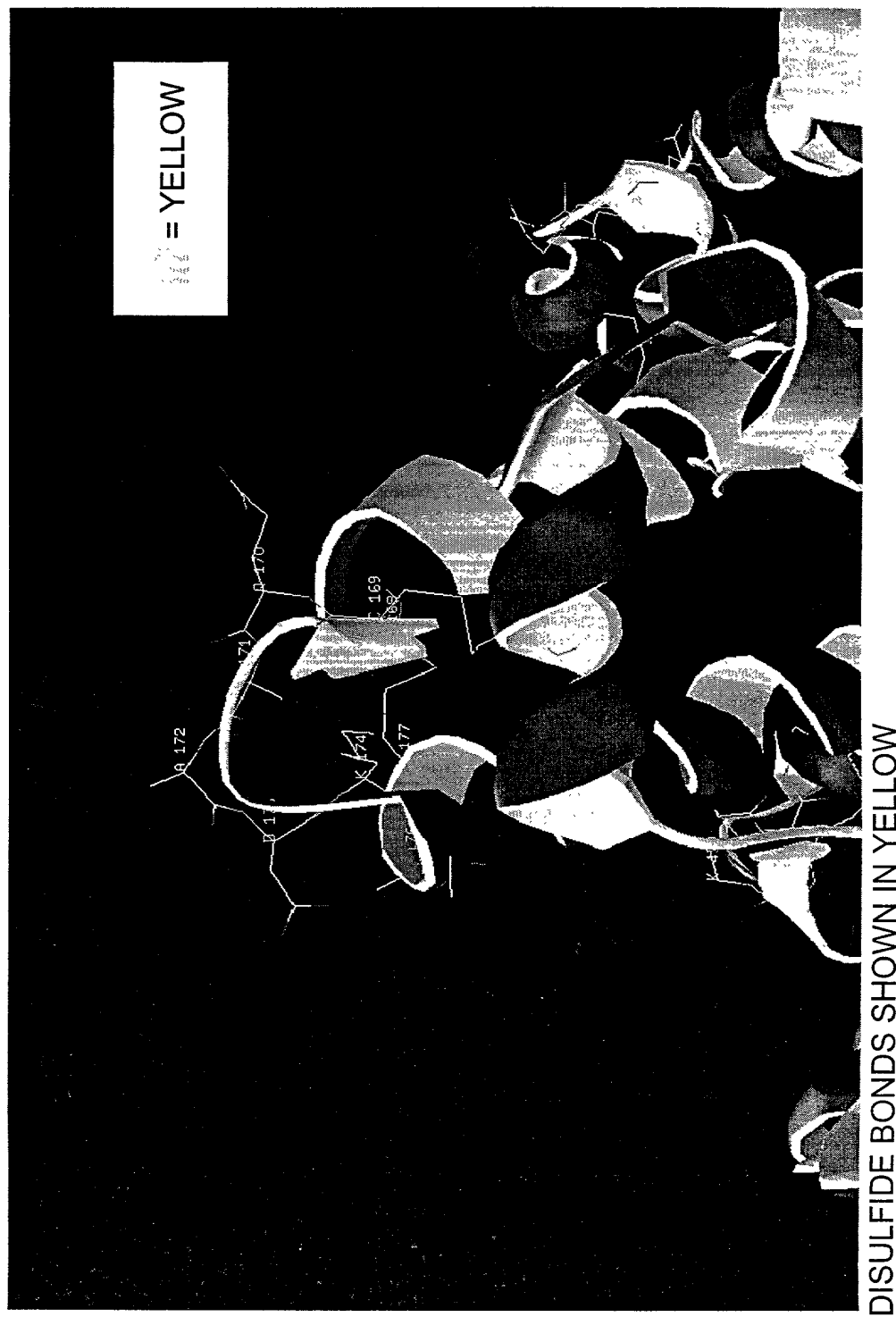


FIG. 12:
LOOP IV GLU170-A176

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HSA [1147 * 084]

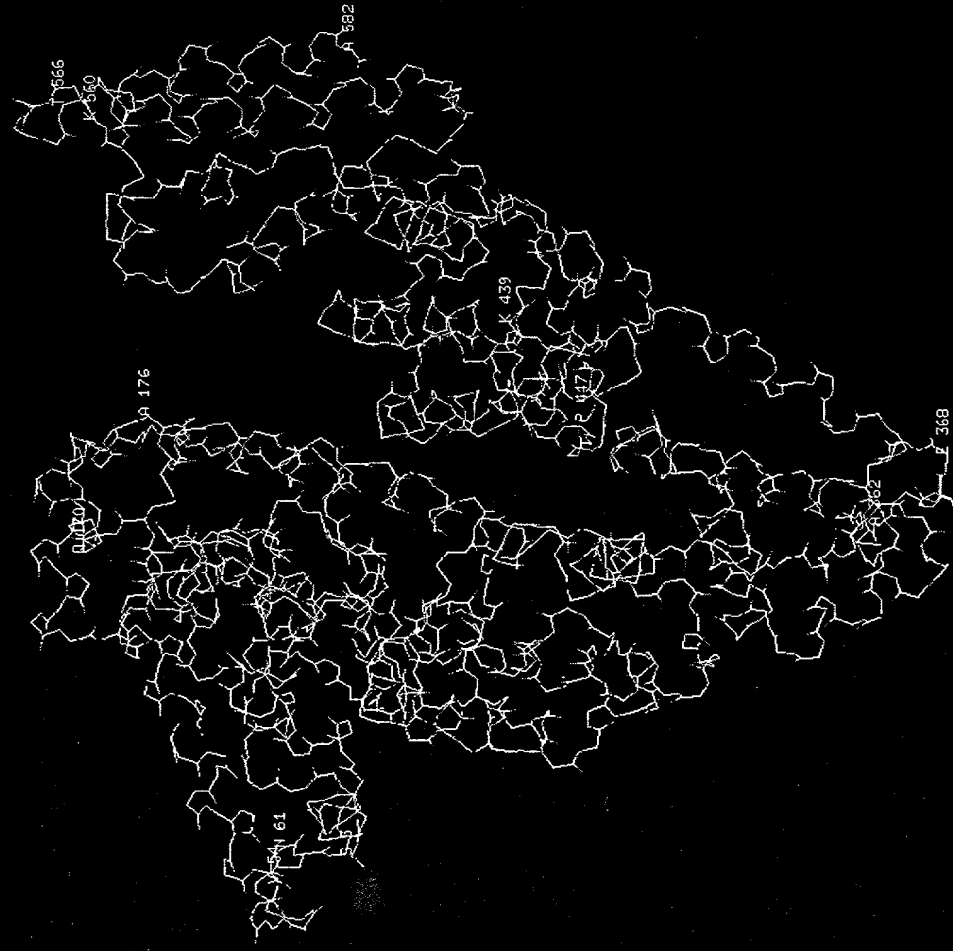


FIG. 13
 TERTIARY STRUCTURE OF HA

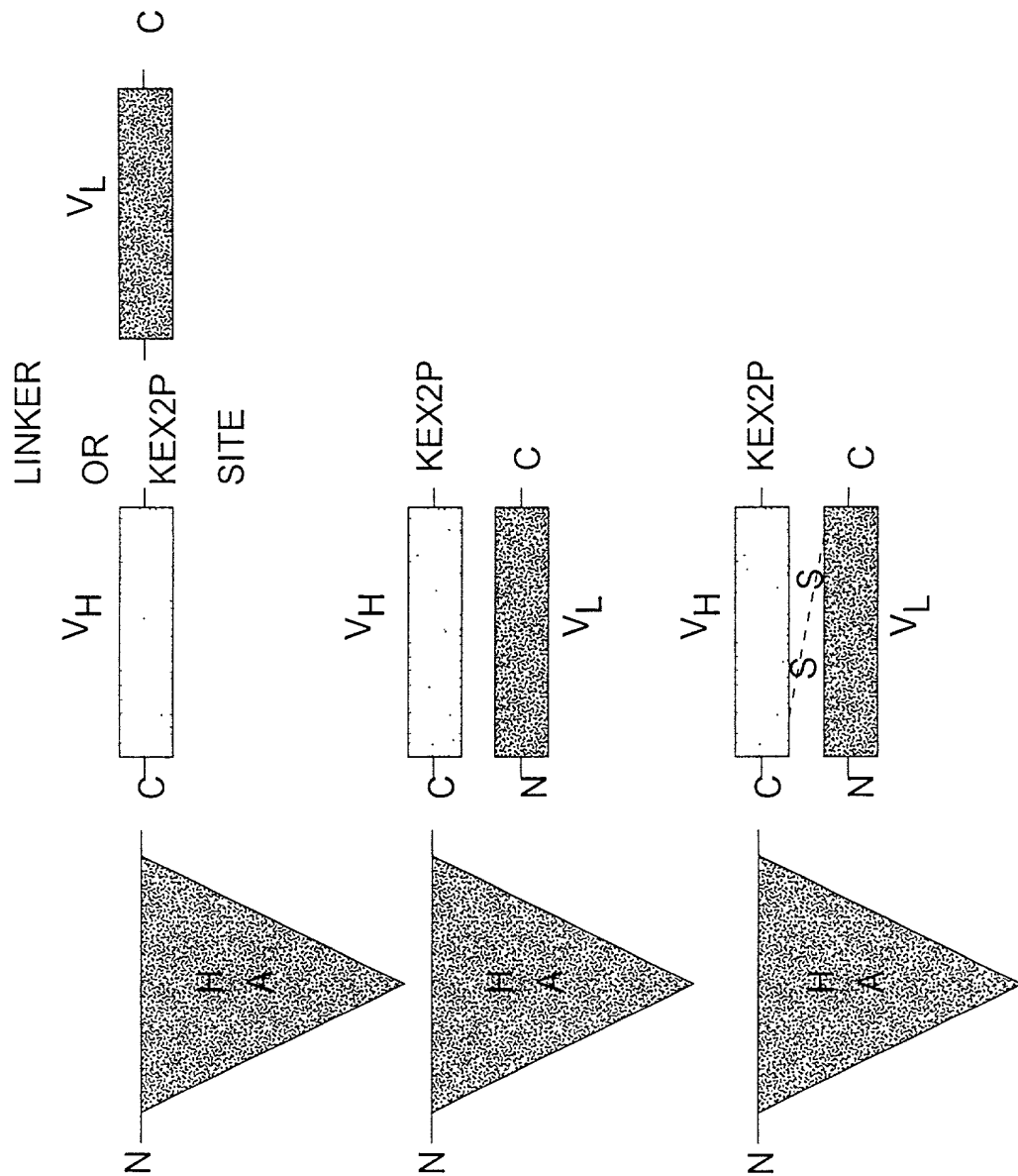


FIG. 14

1 GAT GCA CAC AAG AGT GAG GTT GCT CAT CGG TTT AAA GAT TTG GGA GAA AAT TTC AAA 60
1 D A H K S E V A H R F K D L G E E N F K 20

61 GCC TTG GTG TTG ATT GCC TTT GCT CAG TAT CTT CAG CAG TGT CCA TTT GAA GAT CAT GTA 120
21 A L V L I A F A Q Y L Q C P F E D H V 40

121 AAA TTA GTG AAT GAA GTA ACT GAA TTT GCA AAA ACA TGT GTT GCT GAT GAG TCA GCT GAA 180
41 K L V N E V T E F A K T C V A D E S A E 60

181 AAT TGT GAC AAA TCA CTT CAT ACC CTT TTT GGA GAC AAA TTA TGC ACA GTT GCA ACT CTT 240
61 N C D K S L H T L F G D K L C T V A T L 80

241 CGT GAA ACC TAT GGT GAA ATG GCT GAC TGC TGT GCA AAA CAA GAA CCT GAG AGA AAT GAA 300
81 R E T Y G E M A D C C A K Q E P E R N E 100

301 TGC TTC TTG CAA CAC AAA GAT GAC AAC CCA AAC CTC CCC CGA TTG GTG AGA CCA GAG GTT 360
101 C F L Q H K D D N P N L P R L V R P E V 120

361 GAT GTG ATG TGC ACT GCT TTT CAT GAC AAT GAA GAG ACA TTT TTG AAA AAA TAC TTA TAT 420
121 D V M C T A F H D N E E T F L K K Y L Y 140

421 GAA ATT GCC AGA AGA CAT CCT TAC TTT TAT GCC CCG GAA CTC CTT TTC TTT GCT AAA AGG 480
141 E I A R R H P Y F Y A P E L L F F A K R 160

Figure 15A

481 TAT AAA GCT GCT TTT ACA GAA TGT TGC CAA GCT GCT GAT AAA GCT GCC TGC CTG TTG CCA 540
161 Y K A A F T E C C Q A A D K A A C L L P 180

541 AAG CTC GAT GAA CTT CGG GAT GAA GGG AAG GCT TCG TCT GCC AAA CAG AGA CTC AAA TGT 600
181 K L D E L R D E G K A S S A K Q R L K C 200

601 GCC AGT CTC CAA AAA TTT GGA GAA AGA GCT TTC AAA GCA TGG GCA GTG GCT CGC CTG AGC 660
201 A S L Q K K F G E R A F K A W A V A R L S 220

661 CAG AGA TTT CCC AAA GCT GAG TTT GCA GAA GTT TCC AAG TTA GTG ACA GAT CTT ACC AAA 720
221 Q R F P K A E F A E V S K L V T D L T K 240

721 GTC CAC ACG GAA TGC TGC CAT GGA GAT CTG CTT GAA TGT GAT GAC AGG GCG GAC CTT 780
241 V H T E C C H G D L L E C A D D R A D L 260

781 GCC AAG TAT ATC TGT GAA AAT CAG GAT TCG ATC TCC AGT AAA CTG AAG GAA TGC TGT GAA 840
261 A K Y I C E N Q D S I S S K L K E C E 280

841 AAA CCT CTG TTG GAA AAA TCC CAC TGC ATT GCC GAA GTG GAA AAT GAT GAG ATG CCT GCT 900
281 K P L L E K S H C I A E V E N D E M P A 300

901 GAC TTG CCT TCA TTA GCT GCT GAT TTT GTT GAA AGT AAG GAT GTT TGC AAA AAC TAT GCT 960
301 D L P S L A A D F V E S K D V C K N Y A 320

Figure 15B

961	GAG	GCA	AAG	GAT	GTC	TTC	CTG	GGC	ATG	TTT	TTG	TAT	GAA	TAT	GCA	AGA	AGG	CAT	CCT	GAT	1020
321	E	A	K	D	V	F	L	G	M	F	L	Y	E	Y	A	R	R	H	P	D	340
1021	TAC	TCT	GTC	GTG	CTG	CTG	AGA	CTT	GCC	AAG	ACA	TAT	GAA	ACC	ACT	CTA	GAG	AAG	TGC	1080	
341	Y	S	V	V	L	L	R	L	A	K	T	Y	E	T	T	L	E	K	C	360	
1081	TGT	GCC	GCT	GCA	GAT	CCT	CAT	GAA	TGC	TAT	GCC	AAA	GTG	TTC	GAT	GAA	TTT	AAA	CCT	CTT	1140
361	C	A	A	A	D	P	H	E	C	Y	A	K	V	F	D	E	F	K	P	L	380
1141	GTG	GAA	GAG	CCT	CAG	AAT	TTA	ATC	AAA	CAA	AAC	TGT	GAG	CTT	TTT	GAG	CAG	CTT	GGA	GAG	1200
381	V	E	E	P	Q	N	L	I	K	Q	N	C	E	L	F	E	Q	L	G	E	400
1201	TAC	AAA	TTC	CAG	AAT	GCG	CTA	TTA	GTT	CGT	TAC	ACC	AAG	AAA	GTA	CCC	CAA	GTG	TCA	ACT	1260
401	Y	K	F	Q	N	A	L	L	V	R	Y	T	K	K	V	P	Q	V	S	T	420
1261	CCA	ACT	CTT	GTA	GAG	GTC	TCA	AGA	AAC	CTA	GGA	AAA	GTG	GGC	AGC	AAA	TGT	TGT	AAA	CAT	1320
421	P	T	L	V	E	V	S	R	N	L	G	K	V	G	S	K	C	C	K	H	440
1321	CCT	GAA	GCA	AAA	AGA	ATG	CCC	TGT	GCA	GAA	GAC	TAT	CTA	TCC	GTG	GTC	CTG	AAC	CAG	TTA	1380
441	P	E	A	K	R	M	P	C	A	E	D	Y	L	S	V	V	L	N	Q	L	460
1381	TGT	GTG	TTG	CAT	GAG	AAA	ACG	CCA	GTA	AGT	GAC	AGA	GTC	ACA	AAA	TGC	TGC	ACA	GAG	TCC	1440
461	C	V	L	H	E	K	T	P	V	S	D	R	V	T	K	C	C	T	E	S	480

Figure 15C

1441 TTG GTG AAC AGG CGA CCA TGC TTT TCA GCT CTG GAA GTC GAT GAA ACA TAC GTT CCC AAA 1500
481 L V N R R P C F S A L E V D E T Y V P K 500

1501 GAG TTT AAT GCT GAA ACA TTC ACC TTC CAT GCA GAT ATA TGC ACA CTT TCT GAG AAG GAG 1560
501 E F N A E T F T F H A D I C T L S E K E 520

1561 AGA CAA ATC AAG AAA CAA ACT GCA CTT GTT GAG CTT GTG AAA CAC AAG CCC AAG GCA ACA 1620
521 R Q I K K Q T A L V E L V K H K P K A T 540

1621 AAA GAG CAA CTG AAA GCT GTT ATG GAT GAT TTC GCA GCT TTT GTA GAG AAG TGC TGC AAG 1680
541 K E Q L K A V M D D F A A F V E K C C K 560

1681 GCT GAC GAT AAG GAG ACC TGC TTT GCC GAG GAG GGT AAA AAA CTT GTT GCT GCA AGT CAA 1740
561 A D D K E T C F A E E G K K L V A A S Q 580

1741 GCT GCC TTA GGC TTA TAA CAT CTA CAT TTA AAA GCA TCT CAG 1782
581 A A L G L * 585

Figure 15D